The Office Action returned to applicant a copy of the PTO-Form 1449 with the Galardi, Kimura and Lamanna references lined through indicating that the examiner do not consider these references. Applicant notes that the Lamanna reference was crossed out on the PTO-1449 form, but that the Office Action cited to the Lamanna reference at several places in the Office Action. Nevertheless, applicant includes with this response a resubmitted IDS.

VI. Conclusion

All issues raised by the Office Action have been addressed. Reexamination, reconsideration and allowance of claims 7, 15-17 and 37-38 is requested.

Respectfully Submitted,

Date: April 29, 2002

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CERTIFICATE OF EXPRESS MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this response to the office action and the documents referred to as enclosed herein are being deposited with the United States Postal Service on this date April 29, 2002 in an envelope as "Express Mail Post Office to Addressee" Mailing Label number EL897833735US addressed to BOX RCE, Commissioner for Patents, Washington, D.C. 20231

Susan Bartholomew
Name of person mailing paper

Date: April 29, 2002

Signature of person mailing paper

PLEASE REPLACE PAGE ONE OF THE SPECIFICATION BY THE FOLLOWING UNMARKED PAGE

INTRAPERCARDIAL BOTULINUM TOXIN TREATMENT FOR BRADYCARDIA

by

Stephen Donovan

BACKGROUND

The present invention relates to a method for treating cardiac muscle disorders. In particular, the present invention relates to a method for treating cardiac arrhythmia by administration of a neurotoxin to cardiac muscle.

The pumping action of the heart is controlled by sympathetic and parasympathetic (primarily vagal) nerves which abundantly innervate the heart. Heart rate can be increased by sympathetic stimulation and decreased by vagal stimulation. Additionally, many cardiac fibers, such as the sinus node (also called sinoatrial or SA node) have the capability of self-excitation. Stimulation of the sympathetic nerves causes release of norepinephine at the sympathetic nerve endings. Contrarily, stimulation of the parasympathetic nerves to the heart causes acetylcholine to be released at the vagal nerve endings. Hence, the parasympathetic nervous system is often referred to as a cholinergic system.

The release of acetylcholine by the postganglionic parasympathetic nerve endings, by acting upon the muscarinic receptors present in cardiac muscle tissue, as indicated, decreases the rate of rhythm of the sinus node and decreases the excitability of the AV junctional fibers between the atrial musculature and the AV node, thereby slowing transmission of the cardiac

impulse into the ventricles. The major site of action of parasympathetic control of the heart appears to be the sinoatrial node, where it reduces the heart rate in

VERSION OF PAGE ONE OF THE SPECIFICATION WITH MARKINGS TO SHOW THE CHANGES MADE

~~METHOD FOR TREATING CARDIAC MUSCLE DISORDERS BY ADMINISTRATION OF~~INTRAPERCARDIAL ~~A~~ BOTULINUM TOXIN TREATMENT FOR BRADYCARDIA

by

Stephen Donovan

BACKGROUND

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impulse into the ventricles. The major site of action of parasympathetic control of the heart appears to be the sinoatrial node, where it reduces the heart rate in

UNMARKED VERSION OF THE CLAIMS

7. A method for treating bradycardia, the method comprising the step of intrapericardial injection of a botulinum toxin to an SA node or to an AV node of a heart of a patient with bradycardia, thereby treating bradycardia.

15. The method of claim 7, wherein the botulinum toxin is botulinum toxin type A and the amount of botulinum toxin type A locally administered to the heart is between about 0.01 U/kg and about 35 U/kg.

16. The method of claim 7 wherein the botulinum toxin is botulinum toxin type A and the amount of botulinum toxin type A locally administered to the heart is between about 0.1 U/kg and about 30 U/kg.

17. The method of claim 7, wherein the botulinum toxin is botulinum toxin A and the amount of botulinum toxin A locally administered to the heart is between about 1 U/kg and about 25 U/kg.

37. The method of claim 7, wherein the botulinum toxin is selected from the group consisting of botulinum toxins types A, B, C, D, E, F and G.

38. A method for treating bradycardia, the method comprising the step of intrapericardial injection of a botulinum toxin type A to an SA node or to an AV node of a heart of a patient with bradycardia, thereby treating bradycardia.

MARKED UP VERSION OF THE CLAIMS

7. A method for treating bradycardia, the method comprising the step of intrapericardial injection of a botulinum toxin to an SA node or to an AV node of a heart of a patient with bradycardia~~cardiac muscle~~, thereby treating bradycardia.

Cancel claim 9.

Cancel claim 10.

15. The method of claim 7, wherein the botulinum toxin is botulinum toxin type A and the amount of botulinum toxin type A locally administered to the heart~~cardiac muscle~~ is between about 0.01 U/kg and about 35 U/kg.

16. The method of claim 7 wherein the botulinum toxin is botulinum toxin type A and the amount of botulinum toxin type A locally administered to the heart ~~cardiac muscle~~ is between about 0.1 U/kg and about 30 U/kg.

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